Graphical user interface, application

Description automatically generated![A picture containing text

Description automatically generated]()

Logo

Description automatically generated

**Remote Ischaemic Conditioning After Stroke 3 (RECAST-3)**

**A multicentre randomised controlled trial**

**Qr code

Description automatically generated**

<https://stroke.nottingham.ac.uk/>

**WE ARE STILL LOOKING FOR ADDITIONAL SITES TO TAKE PART IN THE RECAST-3 TRIAL**

For any further information, or to submit an expression of interest, please contact us at [recast-3@nottingham.ac.uk](mailto:recast-3@nottingham.ac.uk)

|  |  |
| --- | --- |
| **Title** | Remote Ischaemic Conditioning After Stroke 3 (RECAST-3): A multicentre randomised controlled trial |
| **Acronym** | RECAST-3 |
| **Short title** | *Remote ischaemic Conditioning After Stroke Trial 3* |
| **Chief Investigator** | Professor Tim England |
| **Aim** | To perform a multicentre randomised controlled trial assessing remote ischaemic conditioning (RIC) in patients with hyperacute ischaemic stroke |
| **Trial Configuration** | Phase III prospective randomised (1:1) sham-controlled blinded-endpoint parallel-group multicentre trial. |
| **Setting** | Adults with hyperacute ischaemic stroke presenting to ~60 Emergency Departments and Stroke Units in the UK. |
| **Number of participants** | 1300 |
| **Eligibility criteria** | **Inclusion criteria:** Hyperacute ischaemic stroke (<6 hours post onset); primary intracerebral haemorrhage ruled out on baseline clinical neuroimaging; NIHSS score >4 at randomisation; age >18 years  **Exclusion criteria:**  Pre-morbid dependency (modified Rankin Scale, mRS>3); Spontaneous intracranial haemorrhage; Dementia; Coma (GCS <8)); Malignancy; Significant co-morbidity (life expectancy <6 months); BM <3.0mmol/L;  Seizure on presentation unless brain imaging identifies evidence of significant brain ischaemia. |
| **Description of interventions** | **Intervention:** RIC group: 4 cycles of intermittent limb ischaemia - alternating 5 minutes inflation (+25 mmHg above systolic BP) followed by 5 minutes deflation of an automated upper arm blood pressure cuff.  **Comparator:** Sham RIC. An automated upper arm blood pressure cuff is inflated to 20 mmHg for 4 cycles (5minutes inflation/5 minutes deflation).  **Duration of treatment:** First dose (4 cycles of RIC or sham) within <6 hours of onset. Second dose 1-2 hours after the first dose. Twice daily until end day 2; total 4 doses. |
| **Duration of study** | Study Duration: Total trial duration 45 months.  Participant Duration: 90±7 days. |
| **Randomisation and blinding** | Web based randomisation will occur immediately after consent, performed by the investigator taking consent. Randomisation will be 1:1 RIC: placebo, minimised on baseline prognostic factors. Follow-up measures will be performed by assessors blinded to treatment allocation |
| **Outcome measures** | **Primary Outcome**: Death or dependency at day 90 (modified Rankin Scale [mRS], ordinal shift analysis) recorded using central blinded telephone follow-up.  **Secondary outcomes** (day 90): Cerebrovascular events; major adverse cardiac and cerebral events; acute kidney injury; disability; cognition; mood; frailty; quality of life; safety (death; neurological deterioration; intracranial haemorrhage, systemic embolism, serious adverse events)  **Mechanisms**: Ischaemic reperfusion injury (Day 2 CT brain: intracranial haemorrhagic, swelling of original stroke, recurrent ischaemic stroke); mechanical thrombectomy substudy (Day 2-7 MRI; infarct growth and volume, oedema, perfusion). |



**Remote ischaemic conditioning (RIC):** An automated upper arm blood pressure cuff is inflated to +25 mmHg above the systolic BP for 4 cycles (5 minutes inflation & 5 minutes deflation).

**Sham:** An automated upper arm blood pressure cuff is inflated to 20 mmHg for 4 cycles (5 minutes inflation & 5 minutes deflation). RIC/sham performed within 6 hours of stroke onset; repeated after 1-2 hours, then twice on Day 2 (once in the morning, once in the afternoon). A total of 4 doses.

**Remote ischaemic conditioning (RIC):** An automated upper arm blood pressure cuff is inflated to +25 mmHg above the systolic BP for 4 cycles (5 minutes inflation & 5 minutes deflation).

**Sham:** An automated upper arm blood pressure cuff is inflated to 20 mmHg for 4 cycles (5 minutes inflation & 5 minutes deflation). RIC/sham performed within 6 hours of stroke onset; repeated after 1-2 hours, then twice on Day 2 (once in the morning, once in the afternoon). A total of 4 doses.

**When are you expecting to restart site set-up?**

We hope to submit the MHRA application and receive the devices in the next few weeks. We will begin set up shortly after and hope to commence recruitment in November 2022.

**How many participants are you expecting each site to recruit?**

Sites should recruit at least 21 patients over the 33 months of recruitment, unless a smaller target has been discussed.

**Are the research team able to obtain consent?**

Yes, we do not need a medic to take consent. Those trained in GCP and the trial procedure, and on the delegation log can consent. You must however have a medic on the delegation log who can review and sign off SAEs.

**Who will conduct the day 90 follow-up?**

The day 90 follow-ups will be conducted centrally by the Follow-up Coordinator in Nottingham. Participants will be contacted by telephone with a postal back-up form if the participant cannot be contacted.

**Does eligibility need to be confirmed by a medic?**

No – eligibility can be confirmed by any member of the research team providing they are appropriately trained on the delegation log to do so. This should be recorded in the medical notes.

**Does treatment need to start within 6 hours of stroke onset?**

The participant **must** be randomised within 6 hours of stroke onset in order to be eligible for the trial. Treatment should also start within 6 hours of stroke onset - if there is a delay between randomising the patient and starting treatment, meaning treatment started after 6 hours, then a protocol deviation will need to be reported.

**What is the payment per participant?**

£52 – a combination of £40 per recruit and £12 for nurse administration time (of the sham). A one-off archiving fee of £200 will be paid to sites at the end of the trial.

**Will sites be paid for performing the 2nd CT scan?**

There is no funding for the repeat CT scan on day 2. In the majority of cases, the second scan will be performed for clinical reasons (post rtPA or MT). It is also performed for safety reasons, even in the non-thrombolysed participants due to potential anti-platelet effects of RIC. Therefore, if the second scan is not performed for clinical reasons, then it is performed for safety reasons and considered a **service support cost (SSC)**. This was discussed and approved with the local CRN prior to the grant application. Sites to liaise with their PI and R&D team to establish whether the 2nd CT scan will be feasible.

**What are the Excess Treatment Costs (ETC) associated with the trial?**

ETCs that should be covered by site amount to £75 per recruit. This should be claimed through the trust’s ETC threshold. For sites that have already reached their ETC threshold, this cost will need to be paid by NHS England.